

IN THE CLAIMS

Please amend claims 16, 20 and 21.

This listing of claims will replace all prior version and listings of claims in the application.

Listing of Claims

1. (Previously presented) A method of treating an individual who has cancer that comprises cancer cells that have a high rate of aerobic glycolysis, the method comprising the steps of:

identifying said cancer as a cancer that comprises cancer cells that have a high rate of aerobic glycolysis, and subsequently

administering to said individual a therapeutically effective amount of an ATP citrate lyase inhibitor, wherein said therapeutically effective amount of ATP citrate lyase inhibitor is sufficient to inhibit ATP citrate lyase activity in said cancer cells to result in inhibition of conversion of citrate into oxaloacetic and acetyl-CoA in said cancer cells, leading to hyperpolarization of mitochondria and increased reactive oxygen species production sufficient to cause said cell to undergo apoptosis.

2. (Original) The method of claim 1 wherein said cancer is determined to be a cancer that comprises cancer cells that have a high rate of aerobic glycolysis by PET imaging.

3. (Original) The method of claim 1 wherein said cancer is determined to be a cancer that comprises cancer cells that have a high rate of aerobic glycolysis by PET imaging using ¹⁸fluoro-deoxyglucose.

4. (Previously presented) The method of claim 1 comprising the step of administering to

said individual a therapeutically effective amount of an ATP citrate lyase inhibitor; wherein said ATP citrate lyase inhibitor is effective to induce apoptosis in greater than 50% of cells in an *in vitro* apoptosis assay at a concentration of less than 1 mM.

5. (Previously presented) The method of claim 1 comprising the step of administering to said individual a therapeutically effective amount of an ATP citrate lyase inhibitor; wherein said ATP citrate lyase inhibitor is effective to induce apoptosis in greater than 50% of cells in an *in vitro* apoptosis assay at a concentration of less than 0.1 mM.

6. (Previously presented) The method of claim 1 comprising the step of administering to said individual a therapeutically effective amount of an ATP citrate lyase inhibitor; wherein said ATP citrate lyase inhibitor is effective to induce apoptosis in greater than 50% of cells in an *in vitro* apoptosis assay at a concentration of less than 50 μ M.

7. (Canceled)

8. (Previously presented) The method of claim 1 comprising the step of administering to said individual a therapeutically effective amount of an ATP citrate lyase inhibitor; wherein said ATP citrate lyase inhibitor is (-) hydroxycitrate.

9. (Withdrawn) The method of claim 1 comprising the step of administering to said individual a therapeutically effective amount of an ATP citrate lyase inhibitor; wherein said ATP citrate lyase inhibitor is SB-204990 shown in Figure 4.

10. (Previously presented) A method of treating an individual identified as having cancer comprising cancer cells that have a high rate of aerobic glycolysis, wherein said cancer comprises cancer cells that have a high rate of aerobic glycolysis and are not dependent on endogenously synthesized fatty acid, said method comprising the steps of:

identifying said cancer as a cancer that comprises cancer cells that have a high rate of aerobic glycolysis, and subsequently

administering to said individual a therapeutically effective amount of an ATP citrate lyase inhibitor, wherein said therapeutically effective amount of ATP citrate lyase inhibitor is sufficient to inhibit ATP citrate lyase activity in said cancer cells to result in inhibition of conversion of citrate into oxaloacetic and acetyl-CoA in said cancer cells, leading to hyperpolarization of mitochondria and increased reactive oxygen species production sufficient to cause said cell to undergo apoptosis.

11. (Canceled)

12. (Previously presented) The method of claim 10 wherein said cancer is determined to be a cancer with cancer cells that have a high rate of aerobic glycolysis by PET imaging.

13. (Original) The method of claim 12 wherein said cancer is determined to be a cancer with cancer cells that have a high rate of aerobic glycolysis by PET imaging using ¹⁸fluoro-deoxyglucose.

14. (Previously presented) The method of claim 10 wherein said ATP citrate lyase inhibitor is administered in conjunction with administration of a different anti-cancer compound.

15. (Previously presented) The method of claim 10 wherein said ATP citrate lyase inhibitor is administered in conjunction with administration of anti-cancer radiation therapy.

16. (Currently amended) ~~A The method of claim 10 further comprising treating an individual identified as having cancer that comprises cancer cells that have a high rate of aerobic glycolysis, the method comprising the steps of:~~

~~identifying said cancer as a cancer that comprises cancer cells that have a high rate of aerobic glycolysis, and subsequently~~

~~administering to said individual a therapeutically effective amount of an ATP citrate lyase inhibitor and, a therapeutically effective amount of a tricarboxylate transporter inhibitor; wherein said therapeutically effective amount of ATP citrate lyase inhibitor and said therapeutically effective amount of a tricarboxylate transporter inhibitor are sufficient to inhibit transport and conversion of citrate into oxaloacetic and acetyl-CoA in said cancer cells cytosol, leading to hyperpolarization of mitochondria and increased reactive oxygen species production sufficient to cause said cell to undergo apoptosis.~~

17-19. (Canceled)

20. (Currently amended) The method of claim ~~16~~ 10 wherein ATP citrate lyase inhibitor is (-) hydroxycitrate.

21. (Withdrawn - Currently amended) The method of claim ~~16~~ 10 wherein said ATP citrate lyase inhibitor is SB-204990 shown in Figure 4.

22-35. (Canceled)

36. (Previously presented) The method of claim 16 comprising the step of administering to said individual a therapeutically effective amount of a tricarboxylate transporter inhibitor, wherein said tricarboxylate transporter inhibitor is selected from the group consisting of: 1,2,3-benzenetricarboxylate, isocitrate, malate, phosphoenolpyruvate, n-butyldmalonate, sulfhydryl reagents, diethyl pyrocarbonate, 2,3-butanedione, phenylglyoxal, pyridoxal, 5-phosphate dicarboxylates, succinate, malate, oxaloacetate, tricarboxylates isocitrate, tricarballylate and palmitoyl-CoA.

37-48. (Canceled)

49. (Previously presented) The method of claim 1 comprising the step of administering to said individual a therapeutically effective amount of a tricarboxylate transporter inhibitor; wherein said tricarboxylate transporter inhibitor is selected from the group consisting of: 1,2,3-benzenetricarboxylate, isocitrate, malate, phosphoenolpyruvate, n-butylmalonate, sulfhydryl reagents, diethyl pyrocarbonate, 2,3-butanedione, phenylglyoxal, pyridoxal, 5-phosphate dicarboxylates, succinate, malate, oxaloacetate, tricarboxylates isocitrate, tricarballoylate and palmitoyl-CoA.

50. (Previously presented) The method of claim 1 comprising the step of further administering to said individual a different anti-cancer compound.

51. (Previously presented) The method of claim 1 comprising the step of further administering to said individual anti-cancer radiation therapy.

52. (Previously presented) A method of treating an individual who has been identified as having cancer that comprises cancer cells that have a high rate of aerobic glycolysis, the method comprising the steps of:

identifying said cancer as a cancer that comprises cancer cells that have a high rate of aerobic glycolysis, and subsequently

administering to said individual a therapeutically effective amount of a compound which inhibits the expression of ATP citrate lyase sufficient to inhibit ATP citrate lyase activity in said cancer cells to result in inhibition of conversion of citrate into oxaloacetic and acetyl-CoA in said cancer cells, leading to hyperpolarization of mitochondria and increased reactive oxygen species production sufficient to cause said cell to undergo apoptosis.

53-57. (Canceled)

58. (Previously presented) The method of claim 52 wherein said cancer is determined to be a cancer with cancer cells that have a high rate of aerobic glycolysis by PET imaging.

59. (Previously presented) The method of claim 52 wherein said cancer is determined to be a cancer with cancer cells that have a high rate of aerobic glycolysis by PET imaging using 18fluoro-deoxyglucose.

60. (Previously presented) The method of claim 52 wherein said cancer comprises cancer cells that are not dependent on endogenously synthesized fatty acid.

61. (Previously presented) The method of claim 52 wherein said ATP citrate lyase inhibitor is administered in conjunction with administration of a different anti-cancer compound.

62. (Previously presented) The method of claim 52 wherein said ATP citrate lyase inhibitor is administered in conjunction with administration of anti-cancer radiation therapy.

63. (Previously presented) The method of claim 52 wherein said cancer is a glioma.

64. (Previously presented) The method of claim 1 wherein said cancer is a glioma.

65. (Previously presented) The method of claim 10 wherein said cancer is a glioma.

66-67. (Canceled)

68. (Previously presented) The method of claim 1 wherein said cancer is selected from the group consisting of glioma, prostate cancer, bladder cancer, renal cancer and lung cancer.

69. (Previously presented) The method of claim 10 wherein said cancer is selected from the group consisting of glioma, prostate cancer, bladder cancer, renal cancer and lung cancer.

70. (Previously presented) The method of claim 10 wherein said ATP citrate lyase inhibitor is effective to induce apoptosis in greater than 50% of cells in an *in vitro* apoptosis assay at a concentration of less than 1 mM.

71. (Previously presented) The method of claim 10 wherein said ATP citrate lyase inhibitor is effective to induce apoptosis in greater than 50% of cells in an *in vitro* apoptosis assay at a concentration of less than 0.1 mM.

72. (Previously presented) The method of claim 10 wherein said ATP citrate lyase inhibitor is effective to induce apoptosis in greater than 50% of cells in an *in vitro* apoptosis assay at a concentration of less than 50 μ M.

73. (Canceled)

74. (Previously presented) The method of claim 52 wherein said cancer is selected from the group consisting of glioma, prostate cancer, bladder cancer, renal cancer and lung cancer.

75. (New) The method of claim 1 further comprising the step of administering to said individual a therapeutically effective amount of a tricarboxylate transporter inhibitor.

76. (New) The method of claim 50 wherein different anti-cancer compound is an anti-cancer antibody.

77. (New) The method of claim 14 wherein different anti-cancer compound is an anti-

cancer antibody.

78. (New) The method of claim 61 wherein different anti-cancer compound is an anti-cancer antibody.

79. (New) A method of treating an individual who has cancer that comprises cancer cells that have a high rate of aerobic glycolysis, the method comprising the steps of:

identifying said cancer as a cancer that comprises cancer cells having a high rate of aerobic glycolysis that are transformed by activation of Akt or by deletion of PTEN, and subsequently

administering to said individual a therapeutically effective amount of an ATP citrate lyase inhibitor.

80. (New) The method of claim 79 wherein said cancer cells having a high rate of aerobic glycolysis that are transformed by activation of Akt,

81. (New) The method of claim 79 wherein said cancer cells having a high rate of aerobic glycolysis that are transformed by deletion of PTEN

82. (New) The method of claim 79 comprising the step of administering to said individual a therapeutically effective amount of an ATP citrate lyase inhibitor; wherein said ATP citrate lyase inhibitor is (-) hydroxycitrate.

83. (New) The method of claim 79 wherein said cancer is a glioma.

84. (New) The method of claim 79 wherein said cancer is selected from the group consisting of glioma, prostate cancer, bladder cancer, renal cancer and lung cancer.

85. (New) The method of claim 79 wherein said ATP citrate lyase inhibitor is administered in conjunction with administration of a different anti-cancer compound.

86. (New) The method of claim 85 wherein different anti-cancer compound is an anti-cancer antibody.

87. (New) The method of claim 79 wherein said ATP citrate lyase inhibitor is administered in conjunction with administration of anti-cancer radiation therapy.